

Application No. 10/658,078

Docket No. 451194-092

Amendment in Response to Office Action mailed September 19, 2005

Page 2

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims of this application:

**Listing of Claims:**

1. (Original) An oral solid pharmaceutical dosage form comprising an extended release (ER) tablet, wherein said ER tablet comprises:

- a. an effective amount of a macrolide antibiotic selected from clarithromycin, azithromycin, or an erythromycin derivative;
- b. from about 2% to about 40% w/w of one or more pharmaceutically acceptable water soluble excipients;
- c. one or more tabletting aids;
- d. wherein the dosage form does not contain a dissolution rate controlling polymer; and
- e. wherein said tablet when tested in a USP Apparatus 2 at 50 rpm using 900 mL 0.1M sodium acetate buffer (pH=5.0) at 37°C exhibits a dissolution profile substantially corresponding to the following pattern:  
not more than 35% of the total antibiotic is released in 2 hours;  
about 30-60% of the total antibiotic is released in 4 hours;  
about 50-90% of the total antibiotic is released in 8 hours; and  
not less than 70% of the total antibiotic is released in 12 hours.

Application No. 10/658,078

Docket No. 451194-092

Amendment in Response to Office Action mailed September 19, 2005

Page 3

2. (Original) A pharmaceutical dosage form as defined in claim 1, wherein said dissolution profile substantially corresponds to the following pattern:

not more than 30% of the total antibiotic is released in 2 hours;

about 30-50% of the total antibiotic is released in 4 hours;

about 60-85% of the total antibiotic is released in 8 hours; and

not less than 85% of the total antibiotic is released in 12 hours.

3. (Previously presented) A pharmaceutical dosage form as defined in claim 2, wherein said tablet core is prepared by (1) granulating clarithromycin, at a concentration of from about 62% to about 90% w/w based on the total tablet weight with a pharmaceutically acceptable filler selected from the group consisting of lactose, mannitol, and microcrystalline cellulose, using an aqueous solution of a hydrophilic binder which is optionally acidified with hydrochloric acid to a normality ranging from about 0.005 to about 0.05, (2) blending said granules with a tableting aid selected from the group consisting of magnesium stearate, fine colloidal silicon dioxide, talc, microcrystalline cellulose, lactose and mixture thereof, and (3) compressing the blend into 500 mg or 1000 mg tablets in the weight range of about 575 - 750 mg and 1120-1500 mg, respectively.

4. (Currently amended) A pharmaceutical dosage form as defined in claim 3 wherein the pharmaceutically acceptable filler in the granulation includes lactose and said filler is present at a concentration of from about 5% to about 35% w/w.

5. (Currently amended) A pharmaceutical dosage form as defined in claim 4 wherein said hydrophilic binder is selected from the group consisting of polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, cornstarch, and dextran for granulation at a concentration of from about 1% to about 4% w/w based on the total tablet weight, added either in the dry form or as an aqueous solution of a mineral acid.

Application No. 10/658,078

Docket No. 451194-092

Preliminary Amendment in Response to Office Action mailed 6/27/2005

Page 4

6. (Original) A pharmaceutical dosage form as defined in claim 3 wherein said tabletting aid includes lactose blended at a concentration of about 1-5 % by weight of total tablet weight.

7. (Original) A pharmaceutical dosage form as defined in claim 3 wherein said tabletting aid includes microcrystalline cellulose blended at a concentration of about 1-4 % by weight for a total polymer content of not more than 5% by weight of the tablet.

8. (Previously presented) A pharmaceutical dosage form as defined in claim 3 wherein said tabletting aid is magnesium stearate alone or in combination with talc externally blended at a total concentration of from about 1.0 % to about 10 % by weight.

9. (Previously presented) A pharmaceutical dosage form as defined in claim 3 wherein said tabletting aid is colloidal silicon dioxide externally blended at a concentration of about 0.1-0.5 % by weight of total tablet weight.

10. (Withdrawn) A production method for the preparation of an extended release clarithromycin tablet, comprising the steps of:

- a. preparing a granulation of clarithromycin in a high shear granulator, comprising a pharmaceutically acceptable filler/diluent and an aqueous solution of a binder, optionally acidified using HCl for a normality of 0.005-0.05;
- b. blending said granulation with other non-dissolution rate controlling excipients selected from the group consisting of a glidant, talc, a filler, and a lubricant;
- c. compressing the blend to produce 500 mg or 1000 mg extended release clarithromycin tablets using a rotary tablet press;

wherein the tablet exhibits a dissolution profile that substantially corresponds to the following pattern:

not more than 35%, of the total clarithromycin is released in 2 hours;

Application No. 10/658,078

Docket No. 451194-092

Preliminary Amendment in Response to Office Action mailed 6/27/2005

Page 5

about 30-60%, of the total clarithromycin is released in 4 hours;

about 50-90%, of the total clarithromycin is released in 8 hours; and

not less than 70%, of the total clarithromycin is released in 12 hours.

11. (Withdrawn) The method of claim 10 wherein said clarithromycin-containing tablet core may be provided with a film coat.

12. (Withdrawn) The method of claim 10 wherein said dissolution profile substantially corresponds to the following pattern:

not more than about 30% of the total clarithromycin is released in 2 hours;

about 30-50% of the total clarithromycin is released in 4 hours;

about 60-85% of the total clarithromycin is released in 8 hours; and

not less than about 85% of the total clarithromycin is released in 12 hours.

13. (Previously presented) A pharmaceutical dosage form as defined in claim 3 wherein the tablet core is provided with a film coat.

14. (Previously presented) A pharmaceutical dosage form as defined in claim 2, wherein said tablet core is prepared by (1) granulating the macrolide antibiotic, at a concentration of from about 62% to about 90% w/w based on the total tablet weight with a pharmaceutically acceptable filler selected from the group consisting of lactose, mannitol, and microcrystalline cellulose, using an aqueous solution of a hydrophilic binder which is optionally acidified with hydrochloric acid to a normality ranging from about 0.005 to about 0.05, (2) blending said granules with a tabletting aid selected from the group consisting of magnesium stearate, fine colloidal silicon dioxide, talc, microcrystalline cellulose, lactose and mixture thereof, and (3) compressing the blend into 500 mg or 1000 mg tablets in the weight range of about 575 - 750 mg and 1120-1500 mg, respectively.